PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 689290.237	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/US05/07748	International filing date *(day/month/year)* 08 March 2005 (08.03.2005)	Priority date *(day/month/year)* 08 March 2004 (08.03.2004)
International Patent Classification (IPC) or national classification and IPC IPC: **C12Q 1/68(2007.01);C07H 21/02(2007.01),C07H 21/04** USPC: 435/6;536/23.1,23.5		
Applicant AVALON PHARMACEUTICALS		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *(sent to the applicant and to the International Bureau)* a total of ___ sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) _____ , containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

Date of submission of the demand 04 October 2005 (04.10.2005)	Date of completion of this report 27 November 2006 (27.11.2006)
Name and mailing address of the IPEA/ US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201	Authorized officer Carla Myers Telephone No. 571-272-1600

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Box No. I Basis of the report

1. With regard to the **language**, this report is based on:
   - ☒ the international application in the language in which it was filed.
   - ☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of:
     - ☐ international search (under Rules 12.3 and 23.1(b))
     - ☐ publication of the international application (under Rule 12.4(a))
     - ☐ international preliminary examination (under Rules 55.2(a) and/or 55.3(a))

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:
   - ☒ the international application as originally filed/furnished
   - ☒ the description:
     pages 1-142 as originally filed/furnished
     pages* NONE received by this Authority on _____
     pages* NONE received by this Authority on _____
   - ☒ the claims:
     pages 143-150 as originally filed/furnished
     pages* NONE as amended (together with any statement) under Article 19
     pages* NONE received by this Authority on _____
     pages* NONE received by this Authority on _____
   - ☒ the drawings:
     pages NONE as originally filed/furnished
     pages* NONE received by this Authority on _____
     pages* NONE received by this Authority on _____
   - ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages _____
   - ☐ the claims, Nos. _____
   - ☐ the drawings, sheets/figs _____
   - ☐ the sequence listing (*specify*): _____
   - ☐ any table(s) related to the sequence listing (*specify*): _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages _____
   - ☐ the claims, Nos. _____
   - ☐ the drawings, sheets/figs _____
   - ☐ the sequence listing (*specify*): _____
   - ☐ any table(s) related to the sequence listing (*specify*): _____

** If item 4 applies, some or all of those sheets may be marked "superseded."*

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 5-60

because:

☐ the said international application, or the said claim Nos. _____ relate to the following subject matter which does not require an international preliminary examination *(specify)*:

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _____ are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed *(specify)*:

☒ no international search report has been established for said claims Nos. 5-60

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

- ☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.
- ☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.
- ☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13*ter*.1(a) or (b) and 13*ter*.2.

☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions, and such tables were not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See Supplemental Box for further details

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Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims 1-4	YES
	Claims NONE	NO
Inventive Step (IS)	Claims NONE	YES
	Claims 1-4	NO
Industrial Applicability (IA)	Claims 1-4	YES
	Claims NONE	NO

2. Citations and Explanations (Rule 70.7)

Claims 1-4 lack an inventive step under PCT Article 33(3) as being obvious over Smith et al. Smith et al (col. 6 and 25) disclose a method of identifying anti-neoplastic agents wherein the method comprises: a) contacting a cell containing a gene sequence that is amplified and has an amplifcation ratio of at least 2; b) detecting a change in the amplification of the gene following exposure to the test agent; and identifying a test agent as being an anti-neoplastic agent if there is a change in amplification as a result of treatment with the test agent. With respect to claims 2 and 3, Smith teaches that a change in the amplification of the gene can be monitored by assaying for a decrease in expression or by assaying for a change in copy number (see col. 25). With respect to claim 4, Smith teaches that screening method is performed using cells that are genetically engineered to express the amplified gene sequence (col. 25). Smith does not specifically exemplify methods in which the amplified gene sequence comprises an amplicon containing 8q24.13 sequences. However, Smith (Table 7) teaches that the sequences of 8q24 are amplified in ovarian cancer and that the sequences of 8q24-25 are amplified in small cell carcinoma. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Smith so as to have used cells containing amplified sequences of 8q24 in order to have identified anti-neoplastic agents useful for treating ovarian cancer or to have used cells containing amplified 8q24-25 sequences in order to have identified ant-neoplastic agents useful for treating small cell carcinomas.

Claims 1-4 lack an inventive step under PCT Article 33(3) as being obvious over Smith et al in view of Squire et al. Smith et al (col. 6 and 25) disclose a method of identifying anti-neoplastic agents wherein the method comprises: a) contacting a cell containing a gene sequence that is amplified and has an amplifcation ratio of at least 2; b) detecting a change in the amplification of the gene following exposure to the test agent; and identifying a test agent as being an anti-neoplastic agent if there is a change in amplification as a result of treatment with the test agent. With respect to claims 2 and 3, Smith teaches that a change in the amplification of the gene can be monitored by assaying for a decrease in expression or by assaying for a change in copy number (see col. 25). With respect to claim 4, Smith teaches that screening method is performed using cells that are genetically engineered to express the amplified gene sequence (col. 25). Smith does not specifically exemplify methods in which the amplified gene sequence comprises an amplicon containing 8q24.13 sequences. However, Squire (page 216) teaches that high copy number amplifications centered on MYC at 8q24.12-8q24.13 were observed in osteosarcoma samples. Squire (Table 1) also teaches that 8q24 and 8q24.1-qter are amplified in osteosarcomas. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Smith so as to have used cells containing amplified sequences of 8q24.12-8q24.13 or 8q24.1-qter in order to have identified anti-neoplastic agents useful for treating osteosarcomas.

Claims 1-4 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be used to screen for anti-neoplastic agents.

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Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claims 1-4 are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because claims 1-4 are indefinite for the following reason(s): Claims 1-4 are indefinite because the claims do not recite a clear nexus between the preamble of the claims and the final step of the claims. The claims are drawn to methods for identifying an anti-neoplastic agent. However, the claims recite a final step in which a change in the amplification ratio is detected as indicative of a test compound that is a gene modulating agent. Accordingly, it is unclear as to whether the claimed method is intended to be one for identifying an anti-neoplastic agent or one for identifying a gene modulating agent.